Nemours Research Programs
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Professor Nirenberg,

I am writing to request some NG108-15 cells for a research project that is commencing in our lab. We are interested in the role of heme metabolism in the differentiation and maintenance of muscular tissues especially if it has a role in neuro/muscular interactions.

As you know, heme catabolism has been implicated in neuronal communication (Verma, et al., 1993). The enzymatic activity of heme oxygenase (with the release of CO, biliverdin IX, and iron) may serve as a retrograde signaling mechanism among neurons, and heme catabolism has been implicated in long term potentiation (Zhuo, et al., 1993; Stevens and Wang, 1993), the modulation of cGMP levels in neurons (Vincent et al., 1994), neurofibrillary pathology in Alzheimer's patients (Smith et al., 1994), as well as carotid body chemoreception (Prabhakar, et al., 1995). In addition, the direct addition of hemin to cultured neuronal cells (Neuro 2a, neuroblastoma cells) has been shown to induce rapid neurite outgrowth (Ishii and Maniatis, 1978).

We wish to investigate the possibility that hemin affects NG108-15 differentiation through the activity of heme oxygenase; further, we wish to determine whether the products of heme catabolism are involved in neuronal differentiation. We plan to compare cellular proliferative activity with measures of cellular differentiation (expression of both choline acetyl transferase and monosialyl-ganglioside, GM2). The effects of hemin and heme oxygenase inhibitors on the proliferation and differentiation of NG108-15 cells will indicate the involvement of heme catabolism in neurite outgrowth in cholinergic neurons. In addition, we will examine the role of heme catabolism in the establishment and maintenance of neuromuscular junctions using co-cultures of NG108-15 cells with cardiac or skeletal muscle cells.

If possible, please send a vial of NG108-15 cells to me at the address given below. Also, please indicate the formulation of the medium which is currently used to propagate the cells as well as what you would consider to be an appropriate "splitting" ratio for propagation of the cells.

I look forward to hearing from you.

cc: Vicki

Sincerely,

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